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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/802,220	03/17/2004	Masaki Sunami	227833	3562

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EXAMINER	
PAGONAKIS, ANNA	

ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
06/26/2012	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Chgpatent@leydig.com

Office Action Summary	Application No.	Applicant(s)	
	10/802,220	SUNAMI ET AL.	
	Examiner	Art Unit	
	ANNA PAGONAKIS	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/30/2012*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-8 and 15-17* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-8 and 15-17* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 sheet, 7/12/2011*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed 1/30/2012 has been received and entered into the present application.

The request to amend inventorship under 37 C.F.R. 1.48(a) filed 4/5/2011 is hereby granted.

Applicant's arguments filed 1/30/2012 have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Status of Claims

Claims 1-8 and 15-17 are currently under examination and the subject matter of the present Office Action.

Rejections necessitated by amendment:

Priority

This application claims benefit of 60/455,293 filed 3/17/2003; 60/460,521 filed 4/4/2003; 60/477,202 filed 6/10/2003 and 60/493,649 filed 8/8/2003.

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications, 60/455,293 filed 3/17/2003; 60/460,521

filed 4/4/2003; 60/477,202 filed 6/10/2003, fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. All claims are not adequately supported or enabled by the prior-filed applications the subject matter in claims 2-5 and 18. Specifically,

(i) 60/455,293 fails to disclose the limitations of claims: 2-7 and 16-17;

(ii) 60/460,521 fails to disclose the limitations of claims: 2-7 and 16-17;

(iii) 60/477,202 fails to disclose the limitations of claims: 2-7 and 16-17;

It is noted that Applicant is not entitled to the priority date in these application for all claims in the instant claim set because the information contained within the previous referred filings does not support the granting of an earlier filing date. Applicant is invited to guide the Examiner to where the appropriate disclosure of the limitations for the above mentioned claims are found the respective priority documents.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ault et al. (U.S. 2002/0123549) in view of Curatolo et al. (WO 2002/11710).

Ault et al. teaches a composition suitable for oral delivery of pharmaceutically active agents, comprising a therapeutically effective amount of a pharmacologically active agent; a crosspovidone or povidone; and a delivery agent for said pharmacologically active agents (abstract). Furthermore, the reference teaches the composition containing crosspovidone versus the comparative compositions which do not contain crosspovidone, resulting the greatly enhanced oral bioavailability of the formulations (paragraph [0084]).

Ault et al. is silent on the increasing the bioavailability of JTT-705.

Curatolo et al. teach that CETP inhibitors, such as the elected compound, S-[2-([[-(2-ethylbutyl)cyclohexyl]carbonyl]amino)phenyl] 2-methyl propanethioate are generally hydrophobic and thus have extremely low solubility and thus have low oral bioavailability (claim 9, page 3). The CETP inhibitor is made in both amorphous and crystalline form, wherein the crystalline form does not exceed 25 percent (page 9). Furthermore, the fraction of CETP inhibitor that is present in relatively pure amorphous domains within the solid dispersion can be relatively small, on the order of less than 20%, and preferably less than 10% of the total amount of CETP inhibitor (page 10). The CETP inhibitors are useful for the treatment of dyslipidemia, hyperbetalipoproteinemia, hypoalphalipoproteinemia, hypercholesterolemia, hypertriglyceridemia, cardiovascular disorders, angina, cardiac ischemia, myocardial infarction, hypertension and obesity (page 7).

One of ordinary skill in the art would have been motivated to substitute the pharmacologically active agent in Ault et al. with that of the claimed compound. One would have been motivated to do so and have a reasonable expectation of success because the claimed

compound is known to have a low oral bioavailability while crospovidone is known to achieve a great enhancement in oral bioavailability.

With respect to claim 7, the ratio of the CETP inhibitor, and crospovidone as well as the amount of crystalline and amorphous forms, it is within the skill of the artisan at the time of the invention and would not have required undue experimentation or have been outside the realm of knowledge generally available to the skilled artisan. Factors that would have been taken into consideration when making such a determination would have included, but not have been limited to, the age, weight, sex, diet and medical condition of the patient, severity of the disease, route of administration, pharmacological considerations, e.g., activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the ratio that would have actually been employed would have been expected to vary widely and, in the absence of evidence to the contrary, would not have been inconsistent with that which is presently claimed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8 and 15-17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 10-11, 16-21, 34-40 and 53-58 of U.S. Patent 7,276,536 (Urata et al.) in view of Ault et al. (U.S. 2002/0123549) in view of Curatolo et al. (WO 2002/11710).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims because the examined claims are either anticipated by, or would be obvious over the reference claims.

The claims of '536 are drawn increasing the bioavailability, increasing the absorption, treatment of a cardiovascular disorder and decreasing LDL with administration of the elected S-[2-([[-(2-ethylbutyl)cyclohexyl]carbonyl]amino)phenyl] 2-methyl propanethioate.

The claims of '536 fail to teach (i) administration with crospovidone; (ii) the crystalline form of to S-[2-([[-(2-ethylbutyl)cyclohexyl]carbonyl]amino)phenyl] 2-methyl propanethioate as well as the AUC and activity of CETP in the bloodstream.

Ault et al. teaches a composition suitable for oral delivery of pharmaceutically active agents, comprising a therapeutically effective amount of a pharmacologically active agent; a crospovidone or povidone; and a delivery agent for said pharmacologically active agents (abstract). Furthermore, the reference teaches the composition containing crospovidone versus the comparative compositions which do not contain crospovidone, resulting the greatly enhanced oral bioavailability of the formulations (paragraph [0084]).

Ault et al. is silent on the increasing the bioavailability of JTT-705.

Curatolo et al. teach that CETP inhibitors, such as the elected compound, S-[2-([[-(2-ethylbutyl)cyclohexyl]carbonyl]amino)phenyl] 2-methyl propanethioate are generally hydrophobic and thus have extremely low solubility and thus have low oral bioavailability (claim 9, page 3). The CETP inhibitor is made in both amorphous and crystalline form, wherein the

crystalline form does not exceed 25 percent (page 9). Furthermore, the fraction of CETP inhibitor that is present in relatively pure amorphous domains within the solid dispersion can be relatively small, on the order of less than 20%, and preferably less than 10% of the total amount of CETP inhibitor (page 10). The CETP inhibitors are useful for the treatment of dyslipidemia, hyperbetalipoproteinemia, hypoalphalipoproteinemia, hypercholesterolemia, hypertriglyceridemia, cardiovascular disorders, angina, cardiac ischemia, myocardial infarction, hypertension and obesity (page 7).

One of ordinary skill in the art would have been motivated to substitute the pharmacologically active agent in Ault et al. with that of the claimed compound. One would have been motivated to do so and have a reasonable expectation of success because the claimed compound is known to have a low oral bioavailability while crospovidone is known to achieve a great enhancement in oral bioavailability.

With respect to claim 7, the ratio of the CETP inhibitor, and crospovidone is within the skill of the artisan at the time of the invention and would not have required undue experimentation or have been outside the realm of knowledge generally available to the skilled artisan. Factors that would have been taken into consideration when making such a determination would have included, but not have been limited to, the age, weight, sex, diet and medical condition of the patient, severity of the disease, route of administration, pharmacological considerations, e.g., activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the ratio that would have actually been employed would have been expected to vary widely and, in the absence of evidence to the contrary, would not have been inconsistent with that which is presently claimed.

Response to Applicant's Remarks

Applicant alleges that the Office fails to provide a credible reason one of ordinary skill in the art would have considered the disclosures of Ault et al. and Curatolo et al. for additional methods of increasing the bioavailability of JTT-705. This is not found persuasive. As stated in the Office Action, one of ordinary skill in the art would have been motivated to substitute the pharmacologically active agent in Ault et al. with that of the claimed compound. One would have been motivated to do so and have a reasonable expectation of success because the claimed compound is known to have a low oral bioavailability while crospovidone is known to achieve a great enhancement in oral bioavailability.

Applicant alleges that the teachings of Curatolo have been mischaracterized. Specifically, Applicant alleges that Curatolo et al. discloses that the amorphous form does not exceed 25% while in fact it appears to state that the crystalline form does not exceed 25%. This is not found persuasive. The teachings of Curatolo cited by the Office Action have been amended in view of Applicant's amended to the claims filed 1/30/2012. In short, as stated above, Curatolo et al. teach that CETP inhibitors, such as the elected compound, S-[2-([[-(2-ethylbutyl)cyclohexyl]carbonyl]amino)phenyl] 2-methyl propanethioate are generally hydrophobic and thus have extremely low solubility and thus have low oral bioavailability (claim 9, page 3). The CETP inhibitor is made in both amorphous and crystalline form, wherein the crystalline form does not exceed 25 percent (page 9).

CONCLUSION

No claim is found to be allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 7am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP

/Brandon J Fetterolf/

Supervisory Patent Examiner, Art Unit 1628